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Título:
Identification of Peptides Targeting Human Osteoarthritic Chondrocytes using Phage Display

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Comunicación:
Osteoarthritis (OA) is one of the most common degenerative joint disease and is characterized by a progressive degradation of articular cartilage extracellular matrix (ECM) leading to loss of joint mobility and function, accompanied by chronic pain. Currently used therapies for cartilage repair are still far from generating regenerated tissue with quality and stability comparable to native cartilage.
We hypothesize that alterations of chondrocyte-ECM interactions in OA affect the expression of cell surface adhesion molecules and phage display can allow the identification of high affinity peptides by screening peptide libraries against these targets. Here, we report the use of phage display to identify novel peptides which specifically bind to human chondrocytes isolated from patients with OA.
Chondrocytes were isolated from healthy and osteoarthritic cartilage obtained from patients undergoing partial knee arthroplasty and characterized, in terms of expression of cell surface proteins and expression of chondrocyte-specific genes, before the panning experiments to assess their phenotypic stage. A phage library displaying random 12-amino acid peptides was first incubated with chondrocytes from healthy donors (control cells) and then with osteoarthritic chondrocytes. A 12-amino acid peptide (GFQMISNNVYMR) was identified, showing high affinity to osteoarthritic chondrocyte cells (about 8-fold higher than the wild-type phage lacking recombinant peptides - control).
Bioinformatics analysis was performed by creating a protein structure database of known and stereo-chemical validated OA-associated cell membrane proteins. Protein-peptide docking revealed, from the overall complex stability, solvent accessibility and binding site prediction that the membrane protein MMP28 is expected to be the putative receptor of the identified peptide ligand.
Future work will be devoted to integrate the identified peptide sequence into nanocarrier systems to provide localization of therapeutic molecules into OA cartilage. If successful, these nanocarriers can offer important insights into the regenerative mechanisms of cartilage and could be applied for developing more efficient and less invasive therapies for treating OA.